Sedation Monitoring & Recovery Training

Lecture notes - Pharmacology of Nitrous Oxide and Scavenging

Objectives and Learning objectives

At the end of the session you should have gain knowledge :-

- Of the physical properties & characteristics of N2O
- On how N2O is absorbed/eliminated
- Of the effects that have N2O have on major organs
- Of the adverse effects/complications of N2O

Inhalation sedation

RA is inhalation sedation using a mixture of nitrous oxide and oxygen
The patient is awake but has a reduced level of fear and anxiety

Properties of an ideal sedative

Predictable
Painless on administration
Immediate onset
Pleasant for the patient
No after effects
Rapid recovery
No side effects

PHARMACODYNAMICS

This is what the drug does to the body

PHARMACOKINETICS

This is what the body does to a drug

Manufacture

Ammonium Nitrate crystals is heated between 250 and 270^{o}C,

NH_4NO_3 -> N_2O + $2H_2O$

purified, and stored in compressed form in metal cylinders

Preparation of N_2O

30% N_2O in liquid form in full cylinder

The pressure gauge (800psi) measures the vapor pressure of the liquid
It exists as a liquid under pressure
800psi - 43.5 bar at 21^{o}C) - that's what is in the cylinders until nearly empty.

Weighing the cylinder is the only way of knowing how much gas is left!!!!!!"!

N_2O E size cylinder weighs 5.4kg empty, 3.37 gas = 8.97kg when full

Physical Properties

- Its one and a half times heavier than air
  (specific gravity 1.53)
- Only inorganic substance other than CO_2 to have CNS depressant properties
- Only inorganic gas used to produce anesthesia in humans
- N_2O constitutes 0.00005% of the earth's atmosphere !!
- N_2O require heat for vaporization into gaseous state
- Relatively insoluble in blood : blood-gas solubility coefficient is 0.47 at 37°C

- Nitrous oxide is carried in simple solution in the body and does not enter into any chemical combination during administration

SOLUBILITY

The Solubility in blood of an agent is expressed as the:-

"BLOOD GAS DISTRIBUTION COEFFICIENT"

The "Blood Gas Distribution Coefficient" is the ratio of the number of molecules of the agent in the blood phase, to the number of molecules in the gaseous phase, per unit volume, at equilibrium.

The solubility of Nitrous Oxide in the blood is an important consideration because it effects the rate of absorption, distribution and rate of excretion.

BGDC for N2O is 0.47 compared to Halothane which has BGDC of 2.36 and Diethyl Ether 12.10

MOVEMENT OF NITROUS OXIDE DOWN PARTIAL PRESSURE GRADIENT

N_2O is rapidly absorbed into the CV due to large concentration gradient of N_2O between alveolar sacs and blood

Absorption

N20 reach the brain by crossing alveolar membranes into the blood
Nitrous oxide is carried in simple solution in the body and does not enter into any chemical combination during administration
CNS saturation occurs by displacement of N_2 by N_2O , usually in 3-5 minutes

Alveolar and grey-matter tension during uptake of 25% nitrous oxide – *diagram see manual*

Absorption

Tissues with:-

greater blood flow (brain, heart, liver, kidney) receive greater amounts of N_2O
poor blood supply (fat, muscle, connective tissue) absorb small amounts

There is no body reservoir present once N2O terminated

The Effects of Nitrous Oxide on organ systems

Cardiovascular system

No changes in heart rate or cardiac output
BP remains stable with only slight decrease
Cutaneous vasodilatation

Respiratory System

N_2O is non-irritating to pulmonary epithelium
Changes drop in respiratory rate and depth more likely due to anxiolytic effects
Slight elevation of resting respiratory minute volume at 50%/50% mix

GI System

No clinically significant effects unless there is an obstruction
N/V rarely seen unless hypoxia present
Can be used in hepatic dysfunction

Hematopoietic System

Long-term exposure greater than 24hrs can produce transient bone marrow depression

Musculoskeletal System

No direct relaxation of skeletal muscle

Anxiolytic effects helps relaxation

Reproductive System

Uterine contraction not inhibited

Pregnancy is a relative contra-indication (avoid 1st trimester)

Actions of Nitrous Oxide

- Nobody really knows the action of N_2O on the CNS
- Latest theory is that it affects the NMDA glutamate receptors
- N-methyl-D-aspartate excite the nerves - opposite to GABA

It blocks their ability to detect a normal sign**al - sedating**

Nitrous Oxide has the following properties and characteristics:-

Anxiolytic properties hence it will reduce the distressing feeling of tension, anxiety , so inducing a state of relaxation and panic

Analgesic It is estimated that a 20% : 80% mixture of N_2O - O_2 produces the analgesic effectiveness of 10-15mg of morphine.

Amnesia Preventing recall of events that occurred after the sedation was given

Weak anesthetic agent

ELIMINATION OF NITROUS OXIDE

Returning with the blood to the left side of the of the heart and are then distributed through the arterial supply to lung.

Hence movement of N2O down partial pressure gradient

Biotransformation

N2O undergoes no biotransformation in the body
Majority of N2O is exhaled unchanged
3-5mins following termination of delivery
1% eliminated via skin and lungs in 24hrs

DIFFUSION HYPOXIA

Rapid diffusion of large volumes of N_2O into the alveoli produces a significant dilution of O_2 present.

- For few minutes on termination of RA the O_2 may drop to 10% !!
- There is a rapid diffusion of N_2O from the blood into the alveoli.
- This decreases CO2 arterial tension with decrease stimulus for respiration and this also dilutes the O_2 present, causes the hypoxia.
- Hypoxia causes headache, nausea, and lethargy-hangover effect.

However

Prevent DIFFUSION HYPOXIA by giving 100% oxygen for 2 - 3 minutes.

POTENCY

Potency is expressed in terms of a **Minimal Alveolar Concentration for an agent (MAC)**

MAC is the concentration of the inhalation anaesthetic required to abolish the response to a standard surgical stimulus in 50% of the patients

Potency of N_2O

N_2O in sub-anaesthetic dosages can produce analgesia
$N_20 + O_2$ at 20:80% mix = 10-15mg of morphine
Optimal concentration is 35%

Properties of an ideal sedative

How does nitrous oxide rate?

Predictable	yes
Painless on administration	yes
Immediate onset	no
Pleasant for the patient	yes
No after effects	yes
Rapid recovery	yes
No side effects	potentially some

Adverse effects Nitrous Oxide

Can be classifies as:-

Acute effects concern the patient

Chronic appear to affect the dentist and assistants

Acute Complications

Excessive perspiration & peripheral vasodilatation *- 2-3% incidence*

If pallor, decreased blood pressure, increased heart rate- consider syncope (100% O2)

Treatment - decrease N20%

Nausea

Causes over sedation - especially >50%
long procedures
anxious patients
inherent tendency
full stomach ??

Treatment decrease N2O

Vomiting

Potentially serious
Could cause aspiration pneumonia, obstruction

Pediatric more often than adult
Early recognition of nausea is key to prevention

Signs of Vomiting

pallor
sweating
cold / clammy
increased salivation
active swallowing

Management of Vomiting

Stop procedure and admin 100% O_2
Remove all dental instruments & rubber dam
Turn head to side
Emesis basin - high volume suction
Replace nasal hood - 100% 0_2 3-5 mins

Shivering

Rare - Usually at end of procedure

Treatment- Reassurance, blanket

Sexual Phenomena

Sexual hallucination/arousal
Females more frequent

Precautions

Always have assistant present
Avoid concentrations >50%
Never leave patient unattended

Adverse effect of CHRONIC exposure

Historically N_2O thought to be inert
1956 Larsen et al – Bone marrow depression in prolong sedation
1968 Banks et al – oxidation of cobalt atom in reduced Vit B12
1976 Ames et al – Linked N_2O exposure to pernicious anaemia

Adverse effects depends on:

Degree and pattern of exposure
Extent to which methionine synthetase is inactivated and the time course of enzymatic recovery
Body store and dietary intake of Vitamin B_{12}
Tissue sensitivity

***Side Effects of <u>CHRONIC</u>* exposure to Nitrous Oxide**

Biochemical effects which

Reproductive problems
Neurological defects
Haematological and immunological problems
Liver problems
Kidney problems
Malignancy
Miscellaneous

Biochemical Effects of Nitrous Oxide Toxicity (Chanari 1980)

N_2O oxidises Vitamin B12
B12 is a co-enzyme needed for the production of methionine
Methionine is an essential amino acid needed for DNA synthesis and maintenance of the myelin sheath
All the observed effects of N_2O exposure can be explained by methionine deficiency

Effects on reproductive system – emotive issue!!!
Concerns relate to increased risk of miscarriage, Conception/fertility - Data is difficult to interpret

" 1995 study of dental nurses suggested if no scavenging then every hour of clinical use resulted in 6% decrease in probability in conception"

Meechan,Robb, Seymours' book on sedation

Concerns relate to increased risk of miscarriage, Conception/fertility

At the present no definitive evidence to suggest brief use of nitrous oxide is harmful to adults and foetus. However at very high levels of unscavenged N2O effects have been found

Weinmann J. 2003

No increased incidence of foetal malformation has been discovered in 8 epidemiological studies in human beings No publish material which shows that N_2O is toxic to human foetus

BOC 2014

Increase in general health problems if chronically exposed to significant levels of unscavenged N_2O. All toxic effects of N_2O are completely reversible upon cessation of exposure to the gas

National Institute for Occupational Safety and Health - NIOSH (2003)

"No conclusive human evidence that exposure to N_2O in the workplace has resulted in increased risk of miscarriage or has caused developmental defects in the foetus."

BDA Advise sheet A3 – Feb. 2008

Epidemiological studies:-
provide strong evidence that there are increased health and reproductive problems among dental personnel chronically exposed to significant levels of unscavenged nitrous oxide.

American Academy of Paediatric Dentistry 2003

Animal studies have demonstrated adverse effects at exposure to high levels so the potential for harm cannot be dismissed

BDA Advise sheet A3 - March 2005

Health and Safety Legislation
Provide and maintain safe equipment, appliances and systems of work
Ensure that dangerous or potentially harmful substances or articles are handled and stored safely
Maintain the place of work in a safe condition
Provide a working environment which is safe without risks to health
Provide the necessary instruction, supervision and training to ensure health and safety

Requirements of the COSHH Regulations include:

COSHH – Nitrous Oxide

- Exposure to hazardous substances should be prevented,
  and where this is not reasonably practicable adequately controlled

  Reduce exposure to as low a level as possible
  Can monitoring level of Exposure by using a monitoring equipment/device

CHRONIC COMPLICATIONS

Occupational exposure

This is a complex issue and a lot of the early concerns regarding occupational exposure to nitrous oxide were born out of the results of animal experiments.
With sensible use, scavenging, and good working practices staff should be able to keep within occupational exposure standards and there should be no adverse effects on our health.

WORKFORCE EXPOSURE LIMITS

Workforce Exposure Levels (WEL) /Occupational Exposure Standards (OSEs)
are based on an 8 hour time weighted average (TWA)
In the UK the WEL /OSE for N_2O = 100 ppm

At this level there are no significant risks to health

The chosen Occupational Exposure Standard of 100ppm is entirely arbitrary

Human studies of exposure to GA
Human studies of exposure to N_2O
Animal studies

UK, Sweden and Norway	100 parts per million (ppm.)
USA and Denmark	25 ppm.

Yagiela (1991) suggests that the minimum threshold for biological effects in man lies well above a continuous exposure of 100ppm for 8hrs period

UNDERSTANDING TIME WEIGHTED AVERAGE (TWA)

During a 3 hour session, air is sampled every 2 min and Occupational Exposure Levels range from 10 – 600ppm with a mean of 250ppm.
8 hour TWA therefore equals 250 X 3/8 = 93.4ppm
But
if operator works 2 sessions per day
TWA = 186.8ppm

Providing the average exposure over 8 hours does not exceed 100ppm, you will be below the chosen Occupational Exposure Standard of 100ppm

Short term peaks are acceptable and inevitable.

Staff considerations

The following personel should avoid exposure to N_2O:-
Female in 1st trimester of pregnancy

Infertile individuals on IVF treatment
Immunocompromised
Neurological complaints

THE IMPORTANCE OF SCAVENGING

Why is it necessary
Why use it?
What is it?
What are the benefits?

SOURCES OF EXPOSURE

Not Scavenged but vented into the local environment
Leakage from breathing delivery system ie mask
Leakage from circuit
Exhaled breath

CONTROL MEASURES

SCAVENGING

- active
- passive

GOOD WORKING PRACTICES

SCAVENING

PASSIVE alone will achieve UK standard of 100ppm TWA with sensible intermittent use

ACTIVE will achieve UK standard of 100ppm TWA

VENTILATION

Increase ventilation in surgery - 6-7 air changes per hour
open window
Extractor fan

Active Scavenging can achieve < 100ppm

Scavenging Systems Efficiency

Porter Brown 71-91% <50ppm

In Summary:-

GOOD WORKING PRACTICES

Check equipment for leaks
Good seal of mask - is the bag moving?
Minimise mouth breathing
Minimise patient talking
Minimise levels of Nitrous used
2 minutes oxygen to finish and keep mask on for further 2 minutes

GOOD WORKING PRACTICES cont./-

Check (at least once a week) that scavenging and ventilation equipment are working properly and have it regularly serviced in accordance with the manufacturer's recommendations and at l least every 12 months.

Periodically review how you operate scavenging equipment to ensure that it is being used correctly.

Make sure your employees are aware of the possible risks to their health, understand why scavenging and ventilation are necessary and how to use the equipment properly